REMARKS

In the Office Action of July 14, 2004, claims 40-41, 49-52, 59-60 and 73 were rejected under 35 U.S.C. 112, first paragraph, for failing to provide an adequate written description of the claimed invention. Specifically, the Examiner states that there is insufficient written description in the specification to support the expression "and another molecule" as used in the present claims. The Examiner contends that this expression is not supported by the specification since the relevant identifying characteristics of the molecule, such as structure or other physical or chemical characteristics, are not set forth. This ground of rejection is respectfully traversed.

The present claims are directed to methods for treating atherosclerosis, methods for inhibiting the formation of atherosclerotic lesions, and methods for treating restenosis. All of these methods utilize chimeric constructs comprising P-selectin glycoprotein ligand-1 in combination with another molecule. The claims state that the chimeric constructs are capable of inhibiting the interaction of P-selectin and a ligand of P-selectin. The present specification, at pages 7 and 8, states that "inhibition" means that P-selectin and its ligand are rendered incapable of properly binding to each other, and provides examples of the inhibitory effects. At pages 8 and 9, the specification also states that the chimeric molecule must be soluble, and provides examples of soluble forms of P-selectin. U.S. Patent 5,834,425, cited by the Examiner, also discloses the formation of chimeric molecules involving P-selectin, and shows the level of skill in the art regarding the preparation and use of chimeric selectins.

The Examiner argues that the claims do not provide sufficient structural and functional characteristics, coupled with a known or disclosed correlation between function and structure, to support the genus of "another molecule". In support of this, the Examiner cites the Guidelines for the Examination of Patent Applications Under 35 U.S.C. ¶112, which sets forth guidelines for the "written description" requirement. The Examiner further states that applicants have not shown possession of the genus of "another molecule" as recited in the claims.

Applicants respond by noting that they are not claiming such a genus of compounds. Rather, the present claims are directed to methods for using chimeric molecules which include P-

selectin glycoprotein ligand-1 and another molecule. The term "another molecule" is not open ended as implied, but must be capable of binding to P-selectin to form a soluble chimeric construct. This is a functional characteristic. Solubility is a physical characteristic, and the fact that the molecule contains, as a component thereof, P-selectin glycoprotein ligand-1 is a structural feature. The soluble chimeric construct has the additional functional characteristic that it must be capable of inhibiting the interaction between P-selectin and a ligand of P-selectin. Thus, the chimeric constructs of the present invention have physical, structural and functional characteristics.

The Guidelines, in referring to the written description requirement, state that the requirement can be satisfied by the disclosure of relevant identifying characteristics, such as structure, physical and functional characteristics, or some combination of such characteristics. The important thing is to put one skilled in the art in possession of the claimed invention at the time of filing, and every feature of the invention need not be specifically disclosed (See Guidelines, page 32641).

As an example, the Guidelines state that it is unnecessary to disclose the complete structure of a DNA molecule so long as sufficient identifying characteristics regarding the molecule are provided, such as physical and chemical characteristics. As an additional example, the Guidelines state that a protein satisfies the written description requirements even though the structure of the protein is not disclosed.

In one particular example cited in the Guidelines, the N-terminal amino acid structure of a protein is described as being enabled even though this is the sole structural feature of the overall molecule. The molecule does have several other identifying characteristics, such as protein function. This example is directly analogous to the supporting disclosure in the present application. See the Guidelines, pages 32641-32642.

Finally, applicants note that the present claims are directed to methods for the treatment of diseases, rather than compositions of matter. Applicants submit that a substantial part of the legal precedent discussed in the Office Action and the Guidelines is applicable only to composition of matter claims, where actual structures are claimed, rather than treatment claims, where only uses of molecules are claimed.

For all of these reasons, applicants submit that the present claims are in full compliance with the written description requirements of 35 U.S.C.112, first paragraph, as well as the requirements set forth in the Guidelines.

Claims 40, 41, 49-52, 59, 60 and 73 are deemed to be unpatentable under 35 U.S.C. 103(a) as obvious over Cummings et al. (U.S. Patent No. 6,309,639) in view of Tedder et al. (U.S. Patent No. 5,834,425), Coller et al. (U.S. Patent No. 5,976,532), and Sluiter et al. (Journal of Cardiovascular Pharmacology; 22 Supplemental 4). This ground of rejection is respectfully traversed.

The Examiner states that the Wagner declaration is insufficient to establish that the claimed invention was conceived and reduced to practice prior to the effective date of the Cummings et al. reference.

As discussed in prior responses, applicants position remains that the Wagner declaration adequately sets forth sufficient evidence to enable one skilled in the art to conclude that the invention described in present claims 40, 41, 49-52 and 59 was conceived and diligently reduced to practice prior to the effective date of Cummings, et al. The statement made in the declaration concerning macrophages and Padgem is fully explained in the declaration.

The Examiner has also criticized the declaration based on the fact that it does not adequately address the invention embodied in present claim 73, which, as correctly noted, is directed to the treatment of restenosis, not atherosclerosis.

Applicants agree that the information supplied in the declaration does not relate directly to restenosis. However, since the Cummings et. al. also does not relate to restenosis, it is entirely unnecessary to antedate Cummings et al. as it applies to claim 73.

Cummings et al. discloses various methods for inhibiting an inflammatory response and for inhibiting leukocyte adhesion using compounds that interfere with the binding of P-selectin. Among the compounds listed in the reference are P-selectin ligand, including the glycoprotein ligand, as well as antibodies to the ligand. Among the disorders listed in the reference are reperfusion injuries, ischemia, sepsis, adult respiratory syndrome, cancer, atherosclerosis and rheumatoid arthritis. See cols. 18 and 19 of the reference.

With respect to atherosclerosis, Cummings et al. states that the rupture of atherosclerotic plaque may lead to thrombus formation and ischemia. See col. 19, lines 57-64. Thus, Cummings et al. does not teach the use of PSGL-1 chimeras to treat atherosclerosis. Rather, Cummings et al. discloses the treatment of the inflammatory condition resulting from the rupture of atherosclerotic lesions or plaque occurring after the disease (atherosclerosis) has progressed to its end stages. This is distinct from the invention recited in present claims 40, 41, 49 and 50, which is directed to preventing the formation or growth of atherosclerotic lesions, i.e. conditions leading to the development of atherosclerosis. Cummings et al. is also silent on the use of vessel-corrective techniques, or the treatment of restenosis as a medical disorder.

Tedder et al. describes chimeric peptides or polypeptides that combine the ligand binding features of the domains of two different selectin molecules. The chimeric molecules of Tedder et al. are used to mediate leukocyte adhesion and function in the circulatory system, and are described as being useful as anti-inflammatory compounds, rather than for treating atherosclerosis or restenosis. There is no disclosure in Tedder et al. that chimeric molecules can be used to treat atherosclerosis or restenosis, or that these molecules can be used to reduce lesions or plaque.

Coller et al. is directed to methods for treating a thrombotic condition in a patient by the administration of a chimeric immunoglobulin directed to the glycoprotein IIb/IIIa receptor. Coller et al. states that the antibodies can be used in a variety of therapies involving thrombus formation, such as embolisms, ischemic attacks, deep vein thrombosis and coronary bypass surgery.

The Examiner has contended that since Coller et al. teaches the use of thrombolytic agents to prevent platelet aggregation and thrombus formation during angioplasty procedures, Coller et al. can be combined with the other references to show that it would be obvious to use the chimeric molecules of the present invention in combination with a surgical procedure. However, as noted above, Cummings et al. is directed to the treatment of acute inflammatory conditions not thrombus formation. Accordingly, there is no factual basis or motivation for combining these references as suggested by the Examiner. Moreover, claims 40, 41, 49 and 50 are directed to decreasing the formation of atherosclerotic lesions in conjunction with a surgical

procedure, and the use of surgical procedures is also not disclosed in Coller et al. or Cummings et al.

The Sluiter et al. literature reference speculates that granulocytes and/or monocytes may play a contributory role in the pathogenesis of coronary restenosis following balloon angioplasty. The reference also states that inflammatory mediators present under such conditions include a variety of well known cytokines, such as IL-1 and TNF-α, and that leuckocyte adhesion molecules, such as P-selectin among others, can also be induced by the activated complement factors. There is no confirming data or any other disclosure in this reference which would lead one skilled in the art to attempt to use a PSGL-1 chimera to treat atherosclerosis or restenosis. In fact, the reference suggests that P-selectin alone can be used in a therapeutic setting. See page S41 of the reference. Consequently, Sluiter et al. adds no meaningful disclosure to the other references cited in the Office Action.

In view of the foregoing facts and reasons, the claims of this application are now believed to overcome the remaining rejections, and to fulfill all remaining requirements for patentability. Accordingly, reconsideration and withdrawal of the rejections, and favorable action on this application, is solicited. The Examiner is invited to contact the undersigned at his convenience to discuss any matter pertaining to this application.

Respectfully submitted,

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